stem cell line (GFP-hES2) was cultured in DMEM/F-12 containing 20% serum replacement, 10% mouse embryonic fibroblast conditioned media and β-Mercaptoethanol on gelatin-coated plates seeded with irradiated mouse feeder cells. *Chondrogenic differentiation:* We developed a novel two step protocol for chondrogenic differentiation of GFP-hES2. 1. Mesoderm differentiation: Embryoid bodies were developed in lo-cluster tissue culture plates in the presence of BMP4, bFGF, and Act-A. 2. Chondrogenesis: The second step was co-culture of the mesodermal cells with primary bovine chondrocytes (bP0). bP0 and GFP-hES2 were mixed at a ratio of 1:4 and co-cultured on Millicell™ membrane inserts, which allow for 3D growth, in DMEM supplemented with 20%FBS. After 4 weeks the newly formed tissue was characterized and compared with tissue formed by bP0 and hES2 alone. **Analysis:** FACS analysis of the GFP-hES2 cells was carried out using selected antibodies. Histological qualitative assessment of the newly formed tissue was done by using light microscopy and toluidine blue staining. Proteoglycan accumulation was semi-quantitatively determined by dimethylmethylene blue dye-binding assay. Values were normalized to total DNA content determined by Hoechst 33258 dye binding assay. Gene expression was quantified by qPCR. **Statistics:** Results were expressed as mean ± SD of 3 independent experiments and significance determined by one-way ANOVA.

Results: FACS analysis after the first stage of culture at day 5 showed that only 5-7% of cells remained positive for ckit, an embryonic stem cell marker, indicating a shift towards more differentiated state. Furthermore, 50-60% of the cells were KDR and PDGF double positive, indicating that these cells attained mesodermal features. At this stage cells were co-cultured with bP0. After 4 weeks GFP-hES2 appeared to be present and surrounded by newly deposited cartilaginous matrix when visualized under fluorescent microscopy. Toluidine blue staining and dimethylmethylene blue assay showed that the proteoglycan content of tissue formed by co-cultured embryonic stem cells at 4 weeks was significantly higher than tissue formed by the bovine chondrocytes alone. qPCR showed higher gene expression of type II collagen, aggrecan, and SOX9. GFP-hES2 cultured alone failed to accumulate any cartilaginous matrix.

Conclusions: We conclude that bovine primary chondrocytes produce factors which promote chondrogenic differentiation of partially differentiated embryonic stem cells. Understanding the mechanism regulating this differentiation may aid in developing a source of cells suitable to use for cartilage repair.

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OSTEOARTHRITIS PATIENTS' PERCEPTIONS REGARDING APPROPRIATENESS FOR TOTAL JOINT REPLACEMENT SURGERY

G. Hawker[1], L. Frankel[1], L. Freeman-Collins[2], D. Marshall[3], B. Conner-Spady[3], C. SanMartin[4]
[1]Univ. of Toronto, Toronto, ON, Canada; [2]Women's Coll. Hosp., Toronto, ON, Canada; [3]Univ. of Calgary, Calgary, AB, Canada; [4]Statistics Canada, Ottawa, ON, Canada

Purpose: Appropriateness criteria for hip/knee total joint replacement (TJR) have been based on expert physician opinion and, in general, consider three groups of patient factors: disease severity (pain and functioning, radiographs), capacity to benefit, and willingness (motivation). The objective of our study was to gain an understanding of patients' perspectives on appropriateness for TJR, including if, and how, appropriateness relates to willingness to undergo this surgery.

Methods: Focus groups were conducted in English-speaking individuals considered good candidates for TJR (WOMAC score ≥ 30/100, x-ray hip/knee osteoarthritis (OA), no surgical contraindications) with and without a prior TJR. Participants were recruited from the community and existing OA cohorts to ensure representation of men and women, urban and rural residents, and ages 40-64 and 65+ years. Focus group questions were directed at understanding participants' perceptions of their own appropriateness for TJR and appropriateness for TJR more broadly, and the relationship, if any, between appropriateness and willingness. Following the discussion, participants completed a standardized questionnaire assessing socio-demographics, arthritis severity (WOMAC), and willingness to consider, and perceived candidacy for, TJR (5-point scales from definitely no to definitely yes). Focus groups were audio-taped and the tapes transcribed verbatim by a single transcriber. Transcripts were reviewed independently by two researchers to identify distinct themes. Themes were compared and consensus reached.

Results: 11 focus groups were conducted in 58 individuals (36 with a prior TJR); mean age was 72 years, 79% were female and 49% had ≤ high school education. Mean symptom duration was 17.5 years. The mean WOMAC summary score was 43.1 (SD 19.8); 50% were willing to consider TJR (75% with and 36% without a prior TJR) and 43% considered themselves appropriate for TJR. Appropriateness for TJR was equated with 'candidacy' for the surgery. Pain intensity, and ability to cope with the pain, was identified as the most important factor determining surgical candidacy, yet participants felt pain was inadequately considered and evaluated by physicians. TJR candidacy was also linked to the balance of risks and benefits, including the impact on employment, independence, and burden on/ability to care for others, their physician's opinion, and comparisons with others who had/had not undergone TJR. Availability of social support and a 'positive outlook' (motivation to comply with post-operative rehab) were identified as key to TJR success, and thus important to consider in assessing appropriateness. Considering these factors, age and weight were felt to be unimportant. Appropriateness and willingness were considered as distinct, yet related, concepts. Participants noted that an individual may feel they are a good surgical candidate, yet be unwilling to consider TJR for other reasons, e.g. care giving responsibilities. However, willingness played an important role in determining patients' sense of appropriateness such that those who were unwilling to consider TJR had stricter rules regarding TJR candidacy than their willing counterparts, seeing TJR as a treatment only for extremes of pain and disability.

Conclusion: Consistent with surgeons, people with hip/knee OA identified arthritis severity, motivation or willingness, and capacity to benefit (risks versus benefits) as key considerations in determining appropriateness for TJR. The patients' pain experience (impact, ability to cope) was seen as the most important determinant, but inadequately considered by clinicians. Enhanced patient-physician communication to better elaborate the OA pain experience, possibly through use of more comprehensive and standardized pain assessment tools, has potential to improve timely access to TJR by those who may benefit.

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FOURTEEN YEAR RISK OF REVISION FOLLOWING PRIMARY TOTAL HIP REPLACEMENT PERFORMED IN A US POPULATION BASED SAMPLE

J.N. Katz[1,2], E.A. Wright[1,2], A.A. Nti[1], J. Wright[1,2], E. Losina[1,2]
[1]Brigham and Women's Hosp., Boston, MA; [2]Harvard Med. Sch., Boston, MA

Purpose: There have been no prior US national population-based studies of the risk of revision following primary total hip replacement (THR) with 14 year follow up and complete ascertainment of revision and mortality. Prior population based studies are limited by substantially incomplete follow-up. It is important to understand the risk of revision among patients undergoing primary THR in order to set appropriate expectations for patients and to accurately forecast resource needs.

Methods: We used Medicare claims data to assemble a cohort of 58,521 patients aged ≥65 who had primary THR in 1995-96. We followed this cohort by assessing their Medicare claims through 2008. We determined the 14 year risk of revision in each cohort, for men and women, using the Kaplan Meier (KM) method. We compared the risk of revision with the risk of mortality over the 14 year time frame. We display these data in two cohorts stratified by age at the time of primary THR: 65-75 and >75.

Results: The 65-75 year old cohort comprised 35,373 THR recipients and the >75 cohort 23,148. 43% of the 65-75 cohort and 75% of the >75 cohort died over 14 years of follow up. The Figures demonstrate the cumulative 14 year risk of revision THR (shown in the darker area on the Figures) and of survival wihtout revision (shown in the lighter area). The two age groups are presented in separate figures. Using the KM method, the cumulative 14 year revision risk in the 65-75 cohort was 14% (16% in males and 13% in females), as compared with a revision risk of 9% in the >75 cohort (11% in males and 8% in females) These differences in sex and age were both statistically significant at $p<0.001$.

Conclusions: In both age groups, particularly those >75, the risk of death was substantially greater than the risk of revision. Revision risk is higher in the 65-75 year old cohort than in those >75 and higher in males than in females. These findings may reflect greater implant wear among males and among younger patients; greater patient preference for proceeding with revision surgery among younger patients and males who have syptomatic loosening; and/or greater willingness among physicians to carry out revision surgery among younger patients. These findings are strengthened by the complete ascertainment of revision and death over the timeframe of the

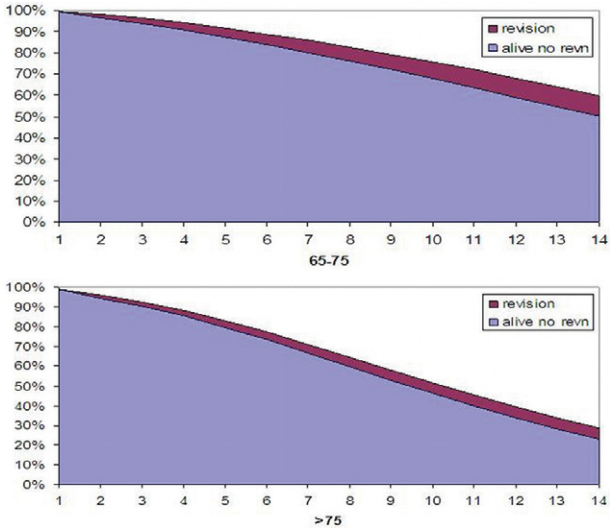

Figure 1. Cumulative risk of revision stratified by age (revision in dark; alive with no revision in light).

study. Future work should confirm and further explicate these findings in databases with more detailed information on clinical features and patient preferences.

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THE USE AND OUTCOME OF HIGH TIBIAL OSTEOTOMY FOR KNEE OSTEOARTHRITIS IN SWEDEN 1998-2007

A. W-Dahl, O. Robertsson, S. Lohmander
Clinical Sci., Lund, Lund, Sweden

Purpose: Unlike for knee arthroplasties, there is no national register on high tibial osteotomies (HTO's) performed in Sweden. Information on the outcome of HTO as a treatment for knee osteoarthritis (OA) is insufficient. The aim of this study was to evaluate the use and outcome, expressed by rate of revision to knee arthroplasty, of HTO's performed in Sweden 1998-2007.
Methods: Using the in-patient and out-patient care registers of the Swedish National Board of Health and Welfare during 1998-2007, patients 30 years or older, with the surgical code NGK 59 (angle, rotation or correction osteotomy in the knee or tibia) in combination with the ICD-10 code M17 (knee osteoarthritis), were identified. The number of surgeries per clinic and County, the gender- and age distribution as well as changes over time were evaluated. Conversion of HTO to knee arthroplasty was identified using the Swedish Knee Arthroplasty Register (SKAR). 446/3,246 HTO's had been converted but for 42 of these side of the the HTO was unknown and thus, if the subsequent arthroplasty had been on the same knee. In these cases we assumed a worst case scenario of the arthroplasty being a conversion. A 10-year survival analysis was performed using revision to an arthroplasty as the end point.
Results: During 1998-2007 3246 HTO (2885 patients) were identified, or 325 per year on average. 8% were out-patient surgeries. During the period there was a 30% decrease in the number of HTO's performed per year. Men had surgery more often (69%) and their mean age at surgery was 52 years (SD 8) as compared to 50 years (SD 7) in women. In 1998, 58% of the patients were younger than 55 years, compared to 65% in 2007, with similar trends for men and women. HTO's were carried out in all Counties of Sweden. Five clinics (out of 75) performed 25% of all the HTO's. As a percentage of all knee reconstructions, HTO decreased from 6% in 1998 to barely 3% in 2007.
The cumulative revision rate (CRR) at 10 years, based on a worst case scenario, was 16% (95% CI 14-24). The risk of revision after adjusting for age was significantly higher in women than men (RR 1.45 (95% CI 1.14-1.83), p=0.002.
Conclusions: In absolute numbers HTO has decreased by 30% during 1998-2007 and constituted less than 3% of the primary knee reconstructions in 2007. HTO was almost exclusively used for patients younger than 65 years. The majority of the HTOs was performed in clinics performing only few surgeries per year. With HTO becoming uncommon, a need to concentrate these surgeries to fewer and more experienced centers should be considered. The rate of conversion to knee arthroplasty was similar to what has been seen for unicompartmental knee arthroplasty.

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JOINT DISTRACTION IN TREATMENT OF CANINE EXPERIMENTALLY INDUCED OSTEOARTHRITIS LEADS TO CARTILAGE REPAIR ACCOMPANIED BY SUSTAINED RELIEVE OF PAIN

S.C. Mastbergen[1], F. Intema[1], P.M. van Roermund[2], H.A. Hazewinkel[3], F.P. Lafeber[1]
[1]Rheumatology & Clinical Immunology, Univ. Med. Ctr. Utrecht, Utrecht, Netherlands; [2]Orthopaedics, Univ. Med. Ctr. Utrecht, Utrecht, Netherlands; [3]Vet. Med., Utrecht Univ., Utrecht, Netherlands

Purpose: Osteoarthritis is a degenerative joint disorder characterized by progressive cartilage damage, peri-articular bone changes, and often secondary joint inflammation. These tissue structure changes coincide with pain, stiffness, and functional disabilities. Few options are available for treatment of end-stage knee osteoarthritis. Eventually, replacement of the affected joint using an endo-prosthesis is currently the accepted treatment option in end-stage osteoarthritis. Joint distraction might be an alternative for a total knee replacement, especially in younger patients. This treatment of osteoarthritis in humans results in long-term clinical benefit. The mechanism responsible for this benefit is unclear. Tissue structure modification was suggested to be involved. Therefore, joint distraction was applied in a canine experimental model of osteoarthritis to study the involvement of cartilage repair.
Methods: Osteoarthritis was induced in the right knee joint according to the Groove model (condylar surgical applied damage) in 16 dogs. Ten weeks post-surgery, the right knee joint was distracted for 3-5 mm by use of a hinged external fixator for 8 weeks in 9 dogs (distraction group). Seven dogs were left untreated (osteoarthritis group). Pain was studied by (un)loading of the joint using force plate analysis every 5-10 weeks. Twenty-five weeks after removal of the external fixators, cartilage integrity of the osteoarthritic, surgically untouched, tibial plateau was analysed.
Results: In the untreated osteoarthritic group, cartilage showed a decreased proteoglycan content (-18%, $p<0.01$), an increased proteoglycan release (+20%, $p<0.03$), and an increase in collagen damage (+2.5%; ns) when compared to the contralateral control joint. This was corroborated by an increased macroscopic and histological grade of cartilage damage (+1.8 and +3.3, respectively, both $p<0.05$). This loss of cartilage integrity was accompanied by decreased loading of the affected joint, especially reflected in a decreased brake and stance force (-0.35N and -0.70N, respectively, both $p<0.05$).
In the osteoarthritic joints treated for 8 weeks with distarction, 25 weeks later, the loss of PG content was -7%, in the distraction group, significantly less ($p<0.02$) decreased compared to the untreated osteoarthritis group, as was the proteoglycan release (+5%; $p<0.05$) which normalized. In addition less collagen damage was found (+0.3%). Again this was reflected in both the macroscopic and histological grade of cartilage damage (+1.3 and +2.8 respectively; $p<0.05$). This relative improvement of cartilage integrity was accompanied by a persistent increase of loading of the treated joint. Both the braking force and stance force normalized ($p<0.05$).
Conclusions: Joint distraction results in less cartilage damage and less pain (based on normalization of loading of the affected knee) in a canine model of experimentaly induced osteoarthritis. The results of this animal in vivo study corroborate the observed cartilage repair and clinical benefit in human studies.

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RECOVERY FOLLOWING TOTAL HIP AND KNEE REPLACEMENT: THE INTERPLAY OF PHYSICAL IMPAIRMENTS, ACTIVITY LIMITATIONS AND PARTICIPATION RESTRICTIONS

A.M. Davis[1], E.M. Badley[1], S. Hogg-Johnson[2], S. Ibrahim[2], A.V. Perruccio[3], R. Wong[1], D.E. Beaton[4], P. Côté[1], M.A. Gignac[1], D. Streiner[5]
[1]Toronto Western Res. Inst., Toronto, ON, Canada; [2]Inst. for Work and Hlth., Toronto, ON, Canada; [3]Harvard and Brigham and Women's Hosp., Boston, MA; [4]St. Michael's Hosp., Toronto, ON, Canada; [5]Kunin-Lunenfeld Res. Inst., Baycrest Hosp., Toronto, ON, Canada

Purpose: Total joint replacement (TJR) is a frequently performed procedure